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EXAMINER
FALK, ANNE MARIE

ART UNIT	PAPER NUMBER
1632	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/656,935	Applicant(s) BLUSZTAJN ET AL.	
	Examiner Anne-Marie Falk, Ph.D.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,11,12,14 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,11,12,14 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

The amendment filed January 2, 2003 (Paper No. 14) has been entered. Claims 7, 9, 11, 12, and 14 have been amended. Claims 1-6, 8, 10, 13, 15, and 16 have been cancelled. Claim 17 has been newly added.

Accordingly, Claims 7, 9, 11, 12, 14, and 17 remain pending in the instant application.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 7, 9, 11, 12, and 14 stand rejected and Claim 17 is rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 3-5 of the Office Action of Paper No. 13 (mailed 10/3/02), as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 is directed to a method for differentiating progenitor cells into cholinergic neurons in a patient by administering a composition comprising BMP-9. Claim 9 is directed to a method for treating degenerating cholinergic neurons in a patient by administering a composition comprising BMP-9. Claim 11 is directed to a method for upregulating the genes for choline acetyltransferase in a patient by

administering a composition comprising BMP-9. Claim 12 is directed to a method for upregulating vesicular acetylcholine transporter in a patient by administering a composition comprising BMP-9. Claim 14 is directed to a method for treating degenerating motor neurons in a patient by administering a composition comprising BMP-9. Claim 17 is directed to a method for treating malfunctioning neurons in a patient by administering a composition comprising BMP-9.

At pages 3-6 of the response, Applicants argue that treatment of a disease is not a requirement of the claims and that the claims are enabled for the *in vivo* effects recited therein. However, the specification does not provide for a specific asserted utility for the claimed methods in the absence of treatment of a disease. On the contrary, the specification asserts that the utility of the claimed invention is for treatment of Alzheimer's Disease (AD) and amyotrophic lateral sclerosis (ALS) (p. 2, lines 11-21). The specification further asserts that the claimed methods can be used in the treatment of conditions exhibiting a degeneration of cholinergic neurons (p. 6, lines 12-15). The Examiner has accepted these statements as credible utilities, albeit ones that are not enabled by the instant specification. Enablement must be evaluated in light of the utility asserted by Applicants.

At pages 3-4 of the response, Applicants refer to the examples of the specification and the specific effects demonstrated in those examples. However, none of the examples constitute working examples of the claimed invention. The teachings of the specification are limited to analysis of embryos injected intracerebroventricularly with BMP-9 (Example I, pages 9-10), analysis of the pattern of expression of BMP-9 mRNA during mouse development (Example II, pages 10-13), and studies of the effect of BMP-9 on cells in culture (Examples III-VIII, pages 10-19). The specification does not provide any working examples with regard to treatment of a diseased animal by administration of a BMP-9 composition.

At page 5 of the response, Applicants point to Barnes et al. (2000) for teaching the treatment of aged rats with an inhibitor of acetylcholinesterase (AChE). Applicants assert that this inhibitor induces

the cholinergic phenotype in much the same way that BMP-9 does, by increasing acetycholine levels. Applicants conclude that Barnes et al. demonstrates that it was within the skill of one in the art to use compounds proven functional in cell culture to treat disease. However, the findings of the study of Barnes et al. do not demonstrate what Applicants conclude, that the compounds under investigation treated disease. On the contrary, the study demonstrates that despite an increase in nicotinic receptor number and hippocampal plasticity mechanisms, there was still no behavioral improvement (p. 22, column 1, paragraph 1). Therefore, no treatment resulted. Furthermore, the drugs administered were donepezil and galantamine, not BMP-9. Thus, the reference does not support enablement for the claimed invention.

At page 6 of the response, Applicants argue that Walton et al. (1999) discloses the delivery of glial cell line-derived neurotrophic factor (GNDF) as a therapeutic agent for neurodegenerative disease. However, the teachings of the reference do not actually disclose treatment of a neurodegenerative disease. Rather it only discloses that GDNF promotes survival of certain neuronal populations. The reference contemplates a therapeutic **potential** for neurodegenerative diseases, but a potential does not constitute an actual treatment effect. It is well-established that an invention must be enabled at the time of filing. Future possibilities for the development of therapeutic protocols do not constitute an enabling disclosure. Furthermore, the agent used was GDNF, not BMP-9. Thus, the reference does not support enablement for the claimed invention.

At page 6 of the response, Applicants argue that Haller et al. (1998) discloses many methods for delivery of proteins to the brain for therapeutic purposes. However, the existence of many methods for distributing drugs throughout brain tissue is not sufficient to enable the instantly claimed invention, because while one of skill in the art could try a wide variety of protocols for administering a protein with the hope of producing a therapeutic effect, given the unpredictability in the art of protein therapy for reasons of record, undue experimentation would have been required for the skilled artisan to develop a

protocol that actually produces the desired therapeutic effect with the agent being used in the presently claimed methods. The specification does not offer the skilled artisan with a starting point that will effect the desired outcome *in vivo* in a diseased animal, nor does it provide the skilled artisan with the direction in which experimentation should proceed.

At page 6 of the response, Applicants allege that the Examiner perceives the invention to solely pertain to the treatment of AD. However, this is incorrect, as the Examiner has repeatedly stated that the claims are broad in scope, encompassing a wide variety of neurodegenerative diseases (p. 4, paragraphs 2 and 3 of the Office Action of Paper No. 13; p. 5, paragraph 1; and p. 5, paragraph 5).

In view of the limited guidance in the specification, the lack of applicable working examples, the unpredictability in the art of therapeutic strategies for neurodegenerative disorders, the broad scope of the claims, and the lack of specific guidance regarding how to use a composition comprising a BMP-9 protein therapeutically to treat a wide variety of neurodegenerative disorder, particularly ALS and AD, undue experimentation would have been required for one skilled in the art to practice the claimed invention, for reasons of record advanced on pages 3-5 of the Office Action of Paper No. 13 (mailed 10/3/02) and as further discussed herein above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite in its recitation of "[a] method for treating degenerating cholinergic neurons in a patient" because no treatment of degenerating neurons is achieved. The claim concludes by reciting induced differentiation of progenitor cells into cholinergic neurons. Thus, the preamble of the claim is in

conflict with the body of the claim. This is a new grounds of rejection necessitated by Applicants' amendment.

Claim 17 is indefinite in its recitation of "[a] method for treating malfunctioning cholinergic neurons in a patient" because no treatment of malfunctioning neurons is achieved. The claim concludes by reciting induced differentiation of progenitor cells into cholinergic neurons. Thus, the preamble of the claim is in conflict with the body of the claim. This is a new grounds of rejection necessitated by Applicants' amendment.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER